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Annals of Physical and Rehabilitation Medicine 57S (2014) e8–e9
ANNALS OF PHYSICAL AND REHABILITATION MEDICINE

Neurosciences INT

Lectures

CO05-001-e

Intravital spectral two-photon microscopy and spinal glass window to study neuroinflammation in spinal pathologies

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Intravital two-photon microscopy has revealed that severed dorsal root ganglions axons have the intrinsic ability to regenerate through the lesion site, especially in highly vascularized areas. The vascular environment indeed exerts a pro-regenerative effect on neurons likely independent of oxygenation and nutrients supply. Yet, perivascular laminin offers a permissive substrate that can promote axon growth as well as the migration of immune cells into the spinal parenchyma. It has been repeatedly shown that resident and peripheral myeloid cells are massively recruited to the spinal cord lesion where they influence the fate of the injury. However, their precise spatiotemporal recruitment dynamics and their respective roles after SCI remain heavily debated due to technical limitations. To clarify these points, we have generated multicolor transgenic fluorescent mice with several populations of labelled immune cells. A spinal glass window methodology has been set up to study the dynamic interactions between immune cell populations and severed/regenerating axons in living mice.
Using chronic quantitative intravital imaging, we have shown that infiltrating LysM (+) and resident CD11c (+) myelomonocytic cells have distinct spatiotemporal recruitment profiles and exhibit phenotypic changes over time. Thus our results underscore the importance of timing and cellular target specificity for developing therapies for SCI.

http://dx.doi.org/10.1016/j.rehab.2014.03.024

CO05-002-e

Cerebral networks for hand dexterity

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The dexterity of the hand in grasping and manipulating objects is one of the distinctive properties of human and non-human primates. Grasping movements involve transforming the visual properties of the object into the coordinated activation of arm and hand muscles to move the upper limb in a coherent way. The cerebral cortex, with its descending corticospinal outputs to the brainstem and the spinal cord is the major structure for the control of grasping movements. We will present a series of studies describing the respective contribution of distinct cortical areas of the parietal and frontal lobes to the control of hand movements. In particular, we will focus on recent technical advances that allow investigating the functional coupling between these cortical structures for upper limb control.

http://dx.doi.org/10.1016/j.rehab.2014.03.025

CO05-003-e

Motor learning principles for neurorehabilitation: Potential of robots for clinical assessment of upper-limb sensorimotor deficits

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In biomedical research, huge progress has been achieved through the development of new technologies. For example, new imaging techniques have permitted important progress in the diagnosis and treatment of various neurological disorders or trauma. These advances reflect the transfer of knowledge and increased use of technology from basic research to clinical practice. However, in this general context, the methods of clinical assessment of motor and sensory deficits in neurology have not substantially evolved, remaining still largely based on clinical tests that do not provide accurate quantification. Today robotic technologies, combined with brain imaging techniques, offer new diagnostic and prognostic tools that could enable the clinicians to design rehabilitation protocols better adjusted to the sensorimotor disorders specific to each patient. I will present recent work in clinical research that exploit experimental paradigms that have been initially developed in fundamental research to explore the basic principles underlying motor adaptation and skill learning in healthy adults. These studies are based on the hypothesis that following a stroke, for instance, the mechanisms involved in the recovery of sensorimotor functions have common bases with those involved in sensorimotor adaptation in the healthy.

http://dx.doi.org/10.1016/j.rehab.2014.03.026

CO05-004-e

New perspectives for the treatment of spasticity and neuropathic pain after spinal cord injury

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Most spinal cord injury (SCI) patients suffer from spasticity and chronic pain. This is a major therapeutic challenge since medical therapies often are ineffective. Recent results from the team suggest that spasticity results from profound modifications of both the intraspinal inhibitory synaptic transmission (decrease in KCC2 chloride transporters and thereby dysregulation of chloride homeostasis, switching the action of GABA/glycine from inhi-

bition to excitation) and the electrical properties of neurons [upregulation of inward persistent currents in motoneurons (MNs) and interneurons]. We tested new pharmacological compounds to restore endogenous inhibition and reduce the excitability of neurons. A translational approach takes us from cellular and molecular levels to the paraplegic animal and finally to patients. We decided to focus on the repositioning of marketed drugs that are approved by the French Drug Agency to speed up the translational process.

http://dx.doi.org/10.1016/j.rehab.2014.03.027